REMARKS

Claims 1-20 were pending in this application when last examined. Claims 4-8 and 13-19 are canceled, claim 1 is currently amended, and new claims 21-24 have been added. Claims 11, 12 and 20 have been allowed.

Support for the amendments can be found in the specification and original claims as file. No new matter has been added.

Support for new claims 21 and 22 can be found in the specification, for example, at page 8, lines 3-4, and in the example formulation at page 4. Support for new claim 23 can be found, for example, at page 6, lines 5-8. Support for new claim 24 can be found, for example, at pages 4-5.

CLAIM REJECTIONS - 35 USC § 103

At page 3, the Office Action rejects claims 1-10 and 13-19 under 35 U.S.C. § 103(a) as being unpatentable over SINGH et al. (US 2003/0185884) in view of FREY (US 2001/0043915), GB 941664 and HATSUYA et al. (US 5342840), and as evidenced by "Resolution Oeno." Applicants respectfully traverse the rejection.

Currently amended claim 1 is directed to a pharmaceutical composition for treating hypoptyalism comprising pilocarpine, a bioadhesive polymer, a buffer, a lubricant, a softening agent, a hydrophilic substance and a hygroscopic

substrate, combined in the form of a tablet. Amended claim 1 includes functional language that further distinguishes over the prior art.

As presently defined in claim 1, the tablet dissolves when placed sublingually in the mouth of a subject and the composition adheres to the mucous tissues in the buccopharyngeal cavity. The pilocarpine then dissolves and binds to muscarine receptors present in the cells of the subject's salivary glands, endobuccal submucous glands and submaxillary glands, and the pilocarpine is then absorbed by the cells, stimulating the glands to produce saliva. The cited references fail to teach or suggest such a pharmaceutical composition in the form of a tablet having the functional characteristics as defined.

SINGH relates to a composition used to raise the pH of the buccal cavity so that pilocarpine can be delivered in a lipophilic form that can then cross the buccal membrane. The delivery composition raises the pH of the buccal cavity through a combination of buffer agents (see, Abstract).

SINGH teaches that "For a substance to be absorbed through the mucosal membrane of the buccal cavity, it has to be presented in a lipophilic form." (See, paragraph [0034]). Thus, SINGH designed a system to deliver pilocarpine in the lipophilic form. For example, SINGH describes a buffer formulation that will "restore free form lipophilicity of pilocarpine and thereby facilitating in vivo absorption via increased permeability."

(See, paragraph [0057]). The SINGH system is based on creating a pH environment that allows the drug to exist in "ready to be absorbed lipophilic form." (See, for example, paragraphs [0040] and [0064]).

In contrast to the teachings of SINGH, the instant claims present a pilocarpine composition that adheres to the mucous tissues in the buccopharyngeal cavity and then allows the pilocarpine to dissolve and bind to the muscarine receptors. The pilocarpine can then cross the buccal mucous membranes to be taken up by the cells in the salivary glands and stimulating the glands to produce saliva. Thus, in contrast to SINGH, the presently claimed composition does not have to alter the pH of the buccal cavity so that pilocarpine can be delivered to the cells.

The present composition includes a combination of components in the form of a tablet, wherein when the tablet is placed sublingually in the mouth the tablet has functional characteristics which lead to pilocarpine absorption by the cells. Those components include pilocarpine, bioadhesive polymer, buffer, lubricant, softening agent, hydrophilic substance and hygroscopic substrate. SINGH fails to teach or suggest that this combination of components could function in the fashion recited by the claims. Indeed, the Office Action recognizes that SINGH fails to teach hyaluronic acid, methylcellulose, lysozyme, polyethylene glycol or disodium hydrogen peroxide. Clearly then,

SINGH cannot teach the claimed combination of components nor their function when together.

SINGH also fails to teach or suggest any specific sub-lingual tablet form of pilocarpine. SINGH is limited to a chewing gum based pilocarpine formulation. Indeed, the pilocarpine chewing gum does not have the functional characteristics of the tablet form as recited in the claims. The chewing gum does not dissolve when placed sublingually in the mouth. Also, the SINGH chewing gum does not adhere to the mucous tissues in the buccopharyngeal cavity. In distinction from SINGH, the presently claimed composition slowly releases pilocarpine under the tongue to be passively absorbed as it is coated by polymers onto the local mucous tissue area. In this way, the present composition induces a local per-mucous contact with the mucous membrane, stimulating the muscarinic receptors of the salivary glands. SINGH fails to teach or suggest this type of sublingual application.

As stated above, the Office Action recognizes that SINGH fails to teach hyaluronic acid, methylcellulose, lysozyme, polyethylene glycol or disodium hydrogen phosphate, and relies on the secondary references in combination with SINGH. The Office Action relies on FREY for teaching tablets with hyaluronic acid, and on HATSUYA for teaching methylcellulose, polyethylene glycol and disodium hydrogen phosphate as tablet components. The Office further relies on GB 941664 and Resolution Ono for teaching

lysozyme in a tablet. The Office then concludes that it would have been obvious to one of ordinary skill in the art to combine all of these components in a tablet. Applicants respectfully disagree with this conclusion.

As detailed above, the presently claimed pharmaceutical composition includes a combination of components that together produce a tablet that when placed sublingually in the mouth the composition adheres to the mucous tissues in the buccopharyngeal cavity, the pilocarpine dissolves and binds to muscarine receptors present in cells of the subject's salivary glands, endobuccal submucous glands and submaxillary glands. The pilocarpine is then absorbed by the cells and stimulates the glands to produce saliva. The functional capability of the combination of components as claimed is not taught or suggested in the cited references.

FREY relates to methods of delivering cytokines to the central nervous system and lymphatic system by way of a tissue innervated by the trigeminal nerve and/or olfactory nerve. FREY's routes of delivery are defined as tissues innervated by the trigeminal nerve, the olfactory nerve or a combination thereof. The cytokine is absorbed through the tissue and transported to the central nervous system of the mammal.

HATSUYA relates to cycloprane derivatives having anti-viral activity but fails to teach or suggest any combination of cycloprane with bioadhesive polymer, buffer, lubricant, softening

agent, hydrophilic substance and hygroscopic substrate, combined in the form of a tablet that functions as presently claimed.

For all of these reasons, SINGH, FREY, GB 941664 and HATSUYA, alone or in any combination, fail to teach or suggest, and would not have rendered obvious, present claims 1-3 and 9-10, as well as new dependent claims 21-24. Claims 4-8 and 13-19 have been canceled. Accordingly, Applicants request reconsideration and withdrawal of the rejection.

CONCLUSION

Entry of the above amendments is earnestly solicited. Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future submissions, to charge any deficiency or credit any overpayment to Deposit Account No. 25-0120 for any

additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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